REMARKS

I. CLAIMS

Upon entry of the foregoing amendment, claims 1-6, 9, 12, 17, 21-23, 26-32 and 34 are pending in the application, with claim 1 being the sole independent claim. Claims 31-32 are currently withdrawn and are being maintained of record pending rejoinder or the filing of one or more divisional applications. Claim 17 is sought to be amended. No new matter is added by way of these amendments. It is respectfully requested that the amendments be entered and considered.

Support for the amendment of claim 17 can be found, *inter alia*, throughout the specification, *e.g.*, page 4, lines 10-17; page 8, line 25 to page 9, line 18; Table 2; and original claims 12-17.

Applicants appreciate and acknowledge that the Examiner has withdrawn the rejections of claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 under 35 U.S.C § 102. (Office Action, pages 3 and 7.)

II. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 17 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite. (Office Action, page 3.) For the purposes of the current Office Action, the Examiner states that "the claim is treated as depending from claim 1." (Office Action, page 3.)

Applicants have amended claim 17 to depend from claim 1. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 17 under 35 U.S.C. § 112, second paragraph.

III. CLAIMED INVENTION IS NONOBVIOUS

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 are rejected under 35 U.S.C. § 103(a) over the teachings of the Lorence references, further in light of the teachings of Curtiss *et al.* (U.S. 7,083,794) and Castracane *et al.* (U.S. 20050074901). (Office Action, pages 3-4.)

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 are rejected under 35 U.S.C. § 103(a) as obvious over Pecora *et al.* (J. Clinical Oncology May 2002, 20(9):2251-2266) in view of Lorence '94 (Lorence B) and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 7.)

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 are rejected under 35 U.S.C. § 103(a) as obvious over WO 00/62735A2 (Lorence C) in view of Lorence '94 (Lorence B) and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, pages 7-8.)

All of the preceding rejections are respectfully traversed below.

To establish a *prima facie* case of obviousness, the Examiner must show that there is a reasonable expectation of success in combining the references. (*In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).)

Applicants believe that the Examiner rejects the claims under 35 U.S.C. § 103(a) because (i) "it was known in the art that successive administration of increasing dosages of various compounds results in increasing tolerance" (Office Action, page 6) and (ii) "it would have been obvious to those of ordinary skill in the art to improve the tolerance of the patients to the virus with additional desensitization administrations" (Office Action, page 8). Applicants respectfully disagree.

There are at least two things that must occur for successful desensitization with a therapeutic negative-stranded RNA virus as claimed herein. First, the administration regimen should cause a desensitization effect in a subject. Second, the subject must not only be desensitized to the therapeutic negative-stranded RNA virus, but the therapeutic virus must retain a therapeutic benefit in the subject. In other words, desensitization or tolerance should not result in negating therapeutic benefit to a subject. However, at the time of the invention one skilled in the art would not reasonably expect that administering sequentially two or more desensitization dose levels of the virus would result in desensitization without negating therapeutic benefit, *e.g.*, for the one or more escalated doses.

For example, the Examiner provides, *inter alia*, Castracane *et al.* as indicating "that it was known in the art that the administration of increasing amounts of various compounds results

in improved tolerance to the compounds. See e.g., . . . Castracane, [paragraph 11]". (Office Action, page 4.) However, this section of Castracane *et al.* states, "increasing doses with time serves to induce tolerance to these agents in patients thereby negating any therapeutic benefit to patients." (Castracane *et al.*, paragraph 11, underlining added.) Therefore, one skilled in the art could not reasonably expect that administering sequentially two or more desensitization dose levels of the virus would result in desensitization without negating any therapeutic benefit of the claimed virus.

The Examiner also cites Curtiss *et al.*, column 18, lines 32-35, which states "[t]he methods of inducing tolerance are well-known and generally comprise administering the allergen to the individual in increasing dosages." However like Castracane *et al.*, Curtiss *et al.* does not meet the second concern, discussed above, that the compound (in this case an allergen) does not retain a therapeutic activity. In this section of Curtiss *et al.*, the therapeutic benefit of administering an allergen is the tolerance/desensitization of the subject to the allergen itself. The subject matter of the present claims relates to desensitization to the virus and the virus retaining a therapeutic activity beyond the desensitization itself.

For the reasons above, the Examiner has not presented evidence that one skilled in the art would consider obvious the sequential administration of two or more desensitization dose levels of a therapeutic negative-stranded RNA virus followed by the administration of one or more escalated doses of the virus. Additionally, the Examiner has not presented evidence that the claimed administration regimen of a therapeutic negative-stranded RNA virus would have had a reasonable expectation of success.

Additionally, Applicants' previous Reply of November 29, 2007 points to the unexpected benefits of using two or more desensitization doses of the virus as compared to the use of one desensitization dose, wherein the amount of the virus in the second and any subsequent desensitization dose is greater than the amount of the virus in the preceding desensitization dose. This result is unexpected since, as discussed above, one skilled in the art at the time of the invention would not have a reasonable expectation that successively increasing doses of the

therapeutic virus would result in both enhanced desensitization while retaining, or even enhancing, a therapeutic effect.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 under 35 U.S.C. § 103(a).

IV. OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for obviousness-type double patenting over claims 1-8 and 11-12 of copending Application No. 10/547,654 ('654 application) in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 9.) Applicants respectfully disagree.

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for obviousness-type double patenting over claims 1-19 of copending Application No. 10/548,057 ('057) in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 9-10.) Applicants respectfully disagree. Claims 1-19 of Application No. 10/548,057 do not describe or suggest administering at least three sequentially increasing dose levels of virus to a subject as required by the presently claimed invention. Also, see relevant discussions related to obviousness in Section III above.

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for obviousness-type double patenting over claims 1 and 5-17 of copending Application No. 10/700,143 in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 10.) Applicants respectfully disagree. Claims 1 and 5-17 of Application No. 10/700,143 do not describe or suggest administering at least three sequentially increasing dose levels of virus to a subject as required by the presently claimed invention. Also, see relevant discussions related to obviousness in Section III above.

The preceding rejections should be withdrawn for an additional reason. The '654 application, the '057 application and the '143 application were filed after the subject application. Accordingly, upon an indication of otherwise allowable subject matter the preceding provisional

obviousnesss-type double patenting rejections should be withdrawn and the subject application should be allowed to issue as a patent without a terminal disclaimer. (MPEP §804(I)(B)(1), Rev. 5, Aug. 2006, page 800-17, right column.)

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for obviousness-type double patenting over claims 118-120, 133, 149 and 150 of copending Application No. 10/167,652 in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 11.) Applicants respectfully disagree. Claims 118-120, 133, 149 and 150 of copending Application No. 10/167,652 do not describe or suggest administering at least three sequentially increasing dose levels of virus to a subject as required by the presently claimed invention. Also, see relevant discussions related to obviousness in Section III above.

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for alleged obviousness-type double patenting over claims 157, 166, 174, 197-201, 210, 217 and 230-232 of copending Application No. 09/958,809 in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 11-12.) Applicants respectfully disagree. Claims 157, 166, 174, 197-201, 210, 217 and 230-232 of copending Application No. 09/958,809 do not describe or suggest administering at least three sequentially increasing dose levels of virus to a subject as required by the presently claimed invention. Also, see relevant discussions related to obviousness in Section III above.

Claims 1-6, 9, 12, 17, 21-23, 26-30 and 34 have been provisionally rejected for alleged obviousness-type double patenting over claims 1-27 of U.S. Patent No. 7,056,689 in view of WO 00/62735 and further in light of the teachings of Curtiss *et al.* and Castracane *et al.* (Office Action, page 12.) Claims 1-27 of U.S. Patent No. 7,056,689 do not describe or suggest administering at least three sequentially increasing dose levels of virus to a subject as required by the presently claimed invention. Also, see relevant discussions related to obviousness in Section III above.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the obviousness-type double patenting rejections.

Conclusion

It is not believed that extensions of time are required beyond those that may otherwise be provided for herein or in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, The United States Patent and Trademark Office is hereby authorized to charge any fee deficiency required to prevent abandonment of the current application or credit any overpayment to Deposit Account 50-1677.

Applicants believe that a full and complete Reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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